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BORDEN'S REVIEW

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CLINICAL STUDIES ON PRENATAL NUTRITION

BORDEN'S REVIEW
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CLINICAL STUDIES ON PRENATAL NUTRITION

"No period in the growth and development of the child has been more neglected than the prenatal period. The groups most interested in maternal and child health have been slow to accept accumulating evidence that improvements in nutrition during pregnancy would result in increased maternal health and a lowered maternal mortality, as well as in marked benefits to child health and development. One reason for this has been the lack of prenatal nutrition studies in which the mother's diet during this important period has been investigated in relation to her course during pregnancy, labor, delivery and her health in the postpartum period, and to the condition of the infant at birth and within the early months and years of life."—*Nutr. Rev. 1,* 81 (1943).

During the past decade a gradually increasing awareness has developed among health authorities with respect to the highly significant role which nutrition plays in the well-being of the expectant mother and in the health and development of the new-born infant. Scientifically controlled studies of the influence of nutrition during the prenatal period are difficult to carry out, particularly when large groups, not subject to close supervision, are involved. As a matter of fact, there have been only five or six major studies along these lines since 1935. While the data thus obtained have been limited in quantity, the implications have been sufficiently conclusive as to stimulate further investigation in this new, specialized realm of nutrition research.

Studies in Great Britain:

In 1935, a committee headed by nine fellows of the Royal College of Obstetricians and Gynecologists was appointed by the People's League of Health to investigate the effect of nutrition of expectant and nursing mothers on maternal and infant mortality and morbidity. About seven years later the committee published a preliminary report on their findings in a survey which covered ten hospitals and included over five thousand women (1).

The plan of their main investigation, carried out during 1938-1939, was to show whether additions of vitamins and minerals to the diet would benefit the course of pregnancy and labor and the newborn child. Diets of the mothers were ascertained through questionnaires. While these data could at best permit only rough estimates of the diets, they did serve to give an approximate idea of the nutritional level of the women. The diets were scored by a system in which arbitrary values were assigned to basic foods (milk, butter,

whole grain bread, fresh vegetables, fish, fruits, eggs, etc.) . A sum of the weekly diet scores served to supply approximate estimates of the intakes of high quality protein, vitamins, minerals and other essentials. By this means it was found that most of the women were obtaining sufficient good quality protein. About 70 per cent of the women, however, had diets deficient in calcium because of an insufficient intake of milk and cheese. As high as 98 per cent were deficient in iron. With respect to vitamins, it was found that more than half were deficient in vitamin A and slightly less in vitamin C. The thiamin intake was fair, but not as high as desirable in almost 50 per cent of the cases.

With this basic information, the women were divided into two main groups. One group received a specially prepared supplement of vitamins and minerals, while the other group served as controls, remaining on their usual diets. The vitamin and mineral supplement, devised on the basis of the probable deficiencies of the diets as revealed by the preliminary survey, provided the following nutrients per day: saccharated iron carbonate, 1.2 grams (equivalent to 2.26 grams of iron) ; calcium lactate, 2 grams (equivalent to 0.26 grams of calcium) ; minute amounts of iodine, manganese and copper; vitamin B complex adsorbate (containing 200 I. U. thiamin per gram as well as other factors of the B complex) ; vitamin C, 100 mg. and halibut liver oil providing 52,000 I. U. of vitamin A and 2500 I. U. of vitamin D per gram. Further classification within both groups was made on the basis of age and number of births, as these factors are statistically significant in influencing the course of pregnancy. The main factors studied were the development of toxemias in the mothers, and prematurity and average birth weight in the infants.

Toxemia of Pregnancy: Toxemia of pregnancy includes a number of morbid conditions ranging from nausea and vomiting through hypertension, nephritis, and in severe instances, convulsions or eclampsia. For purposes of the study in question it was decided to regard as toxemic those women who exhibited hypertension (a systolic blood pressure of 140 mm. Hg or more or a diastolic pressure of 90 or more) with or without albuminuria, and women who exhibited albuminuria with or without hypertension. These criteria were later modified to include only women with albuminuria, since many cases of hypertension alone are often essential hypertension rather than a true form of pregnancy toxemia. The following table illustrates the results obtained with treated and control groups:

—	No. of women	Hypertension only		Albuminuria with or without hypertension		Hypertension with albuminuria, &c. ("pre-eclampsia")	
		No. of cases	Percentage	No. of cases	Percentage	No. of cases	Percentage
Primiparas—							
Treated	1530	332	21·7	83	5·4	69	4·51
Controls	1512	368	24·3	112	7·4	97	6·42
Diff. (C-T), and SE	..	..	2·6 ± 1·5	..	2·0 ± 0·9	..	1·91 ± 0·82
Multiparas—							
Treated	980	79	18·3	35	3·6	31	3·16
Controls	999	166	16·6	52	5·2	46	4·60
Diff. (C-T), and SE	..	..	1·7 ± 1·7	..	1·6 ± 0·9	..	1·44 ± 0·87
Total	5021	1045	...	282	...	243	...

SE = standard error.

From the table it can be seen that the primiparous women (those having their first baby) receiving the dietary supplements had an incidence of toxemia of 5.4 per cent, while the untreated primiparas showed a toxemia rate of 7.4 per cent. Statistical analysis showed that the standard error was 40 to 1 against such a result being obtained by mere chance. In the multiparous group, similar but not as striking results were obtained. In general, it was concluded that the additional dietary supplements protected the women of both groups against the risk of toxemia in a ratio nearly approaching 30 per cent. These findings are highly significant when it is remembered that, next to puerperal sepsis, toxemia constitutes the most important cause of maternal death (about one-fifth the total death rate), in addition to being one of the most fertile sources of chronic ill health after childbirth.

Infant: The value of improved diets during the prenatal period with respect to the infant was also demonstrated in these studies. The most important benefit to the infant was the prevention of prematurity, the cause of one-half of infant deaths in the first month of life. In the primiparas receiving the vitamin and mineral supplemented diet, 20 per cent failed to carry the infant to term, while the incidence of prematurity among the controls was almost 24 per cent. The figures for the multiparas were almost identical.

The differences in birth weight for the treated and control groups were very slight and could not be regarded as statistically significant.

Additional Studies: In February, 1944 another report appeared in the British scientific press on the effect of supplementary feeding in pregnancy. The studies, reported by Balfour (2) were carried out in 28 different areas throughout North England and Wales and included almost twenty thousand women. The experiment started in April, 1937 and was concluded in March, 1939. More than eleven thousand women attending prenatal clinics in impoverished areas were selected for supplementary feeding, while the records of some eight thousand women attending the same clinics, but who did not receive supplements, served as controls.

The supplemented groups received every two weeks a pound and a half of a powdered milk preparation and either four ounces of a special yeast extract (providing 240 I. U. thiamin daily) or eight ounces of a proprietary preparation supplying liberal amounts of vitamins A and D (providing 13,500 I. U. vitamin A and 2,250 I. U. vitamin D daily), phosphorus, calcium and iron. Both supplemented and control groups received some milk distributed by the local health authorities.

The groups were compared statistically as to age, number of births, social and economic condition.* There was a higher proportion of primiparas in the control group, but it was counterbalanced by the much lower proportion of women with a record of ten or more births. Also, there was a smaller proportion of women over 30 in the control group. The treated group consisted of women in extremely poor circumstances, living in crowded unsanitary slum areas; while the controls were better off economically, less crowded and more able to provide food for the children even in larger families. Thus, although the two groups were not strictly comparable, the scales were weighted against the treated group.

Results: The yeast-fed groups and the groups fed the proprietary preparation were considered separately. Those receiving the latter exhibited a lower rate of stillbirths and neonatal deaths than the controls, but the difference was not considered statistically significant. The groups receiving the yeast supplement, however, exhibited a marked difference in rate of stillbirths and neonatal mortality. Statistical analysis showed that the possibility of these results being due to chance was less than 1 in 1300. The effect of the yeast extract was greatest in the localities where the control mortality rates were highest.

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*It has been shown that neonatal death rate is influenced by the parity. It is lowest in the second confinement, and begins to rise in the third. By the fifth it exceeds that of the first and at the tenth and subsequent births, the rate is nearly double that of the first. The neonatal mortality rate is influenced also by the age of the mother, rising rapidly after the age of 30 (3).

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From this study it is apparent that even a small improvement in the diet (about 8 grams of yeast concentrate per day) supplying considerable amounts of thiamin and iron, as well as appreciable amounts of riboflavin and niacin, can effect a marked improvement in the health of the newborn infant.

From the combined results of these studies and of those conducted by the People's League of Health, it has been unequivocally demonstrated that improving the diet of the mother in the prenatal period is of utmost importance to the health of both mother and infant—protecting the former against dangerous toxemias and decreasing, among the latter, the incidence of prematurity, stillbirth and death in the first month of life.

Canadian Studies:

While the studies of Balfour and of the People's League of Health were under way in England, a similar series of studies was being conducted by Ebbs, *et al* (4, 5) in Canada. This study was conducted at the Toronto General Hospital and included almost four hundred women. Careful, detailed analyses were made of the patients' diets which were scored "good," "fair" or "poor." Every alternate patient in the poor diet group was selected for supplementary feeding, thereby forming a Poor Diet Group and a Supplemented Group. Those found to be eating a good diet and economically capable of obtaining a better diet were merely given advice as to how to further improve their diet (Good Diet Group).

Dietary Goals: The following amounts of foods were set up as reasonable daily dietary requirements during pregnancy: 40 ounces (5 glasses) of milk, 1 ounce cheese, 1 egg, 1 serving butter, 1 serving meat, 2 servings vegetables in addition to potato, 1 orange or ½ grapefruit or 5 ounces of tomato juice, one-half of all cereals and bread consumed in whole grain form, 2 teaspoonfuls of cod liver oil or the equivalent, iodized salt and medicinal iron, if indicated. In addition liver once a week was recommended and also 2 tablespoonfuls of wheat germ per day. The composition of this recommended good diet is given in the following table:

Nutritive factors yielded by the recommended Good Diet used in this study.

		Vitamins:	
Calories	— 2400-2800	A	— 6000 I.U.[1]
Protein	— 80-100 gm.	B_1	— 500-1000 I.U. (1.5-3.0 mg.)
Fat	— 80-100 gm.	B_2	— 3.0-3.5 mg.
Carbohydrate	— 350-400 gm.	C	— 50-75 mg.
Calcium	— 1.5 gm.	D	— 500-1000 I.U.
Iron	— 0.020 gm.		
Iodine	— In iodized salt	[1]International Units.	

The patients in the Good Diet Group with sufficient income were advised to obtain the amounts listed in the table. The patients in the Supplemented Group received the following food supplements each day: 30 ounces of milk, 1 egg and 1 orange. Once a week they received two 16-ounce cans of tomatoes and ½ lb. of cheddar cheese. In addition, a wheat germ product containing malt and added iron was supplied and viosterol capsules containing 2000 I. U. of vitamin D were given with instructions to take one daily. The women were carefully advised as to the use of this extra food and were also instructed with respect to planning the rest of the diet from the family income. The nutrients contributed daily by this supplementary food were as follows:

Nutritive factors yielded by the supplements provided.

		Vitamins:	
Calories	— 840	C	— 50-80 mg.
Protein	— 45 gm.	B_1	— 350-400 I. U. (1-1.2 mg.)
Fat	— 46 gm.	D	— 2000 I. U.
Carbohydrate	— 60 gm.		
Calcium	— 1.45 gm.		
Iron	— 15 mg.		

The special dietary advice and supplements were begun about the fourth or fifth month of pregnancy and maintained for one month following delivery.

Results (Mothers): At the end of the experiment it was found that the mothers on the good or supplemented diets enjoyed better health throughout the entire course of pregnancy, had fewer complications and proved to be better obstetrical risks than those left on poor prenatal diets. The incidence of miscarriages, stillbirths and premature births was much higher in the women on poor diets. Further, the babies born of the Poor Diet Group showed a far greater incidence of illness and of deaths therefrom in the first six months of life.

The statistical data reveal that the diets of the Poor Diet Group and the Supplemented Group were equally low in every respect at the beginning of the experiment, while those of the Good Diet Group were fairly good. Analysis of the diets in the second record made shortly before the birth of the babies showed that the diets of the Supplemented and Good Diet groups were considerably improved, the former by receiving food supplements and the latter by education.

In the Poor Diet Group 60 per cent were eating less than 60 gm. of protein daily. In the Supplemented Group 78 per cent were getting more than 80 gm. protein daily after the extra food was supplied.

Advice to those in the Good Diet Group about increasing the consumption of milk, eggs, meat and cheese likewise resulted in an appreciable improvement in the protein intake. The addition of milk and cheese also markedly improved the calcium intake of the two groups. Similar improvement in vitamin C intake was also reflected as a result of advice and the provision of citrus fruits. The thiamin content of the original poor diet in the Supplemented Group was more than doubled by the addition of wheat germ, milk, egg, orange and tomato and by changing from white to whole wheat bread.

Complications of pregnancy correlated with diet.

		POOR DIET	GOOD DIET	SUPPLEMENTED-GOOD DIET
Past obstetrical history of multiparous patients (% of cases):				
Abortions		13.1	9.0	4.7
Miscarriages		38.1	24.4	39.0
Prematures		10.7	13.3	20.3
Stillbirths		9.5	2.2	4.7
Obstetrician's rating during pregnancy (% of cases):				
Prenatal period	Good-Fair	64	88	91
	Poor-Bad	36	12	9
Labor	Good-Fair	76	94	97
	Poor-Bad	24	6	3
Convalescence	Good-Fair	88	91	96
	Poor-Bad	12	9	4
Whole course of pregnancy	Good-Fair	66	85	94
	Poor-Bad	34	15	6
Complications during pregnancy (% of cases):				
Anemia		28.6	21.6	16.1
Preeclampsia		5.0	4.8	5.7
Toxemia		7.6	3.0	3.4
Hemorrhage—prenatal		5.9	2.4	5.7
Threatened miscarriage		8.4	2.4	1.1
Miscarriage		6.0	1.2	0
Premature birth		8.0	3.0	2.2
Stillbirth		3.4	0.6	0
Hemorrhage (during labor)		11.2	7.7	10.3
Endometritis		9.0	6.1	3.4
Mastitis		4.5	4.8	2.3
Breast abcess		3.0	2.0	1.1

Results (Infants): The benefits to the infants resulting from improving the maternal diet during pregnancy are considered in detail in a subsequent report by the Toronto group (6). Rating of the

babies during the first two weeks revealed 14 per cent "poor" or "bad" in the Poor Diet Group, as against none in the Supplemented Group and 4 per cent in the Good Diet Group. ("Poor" or "bad" includes miscarriages, stillbirths, difficult progress, etc.). Slightly more than half the babies in the Poor Diet Group were rated "good" as against 90 per cent in the Supplemented Group. There were considerably more illnesses among the babies in the Poor Diet Group and three deaths, one due to prematurity and two to pneumonia.

Studies in United States:

The special problems of metabolism and nutrition during pregnancy have been studied by a number of investigators in the United States (7, 8, 9, 10, 11, 12). Most of the early studies, both in the United States and abroad, were concerned chiefly with the importance to the mother of adequate nutrition during the prenatal period. Recent studies, however, have brought out the fact that prenatal nutrition may have a very pronounced effect on the condition of the infant. As was pointed out in the British studies, poor maternal diets directly influenced the mortality rate of the newborn, particularly by predisposing to maturity. Other studies, however, have revealed that actual physiological damage to the fetus may result from dietary deficiencies of the mother during gestation. The startling results recorded by animal experimenters on the production of abnormal young by faulty maternal diets have already been reported at length.* Within the past few years, scattered reports of similar fetal damage in humans resulting from prenatal dietary deficiencies have appeared (9, 13, 14, 15). These have included, among others, the appearance of early tooth defects traceable, in part at least, to a deficiency of milk and of cod-liver oil in the maternal diet; the development of fetal and infantile rickets in babies born of mothers suffering from osteomalacia due to insufficiency of calcium, phosphorus and vitamin D.

Of particular interest in this connection is a recent report by Burke *et al* (16, 17) of Boston on the effect of prenatal diet on the infant. In this study, 216 women and their infants were observed at the Center for Research in Child Health and Development. The diets of the mothers during the prenatal period were carefully checked and rated according to standards closely approximating the recent values recommended by the National Research Council. On this basis it was judged that of the 216 cases studied, only 14 per cent consumed diets during pregnancy (4th to 9th month) which could be considered

*Borden's Review of Nutrition Research, November, 1944.

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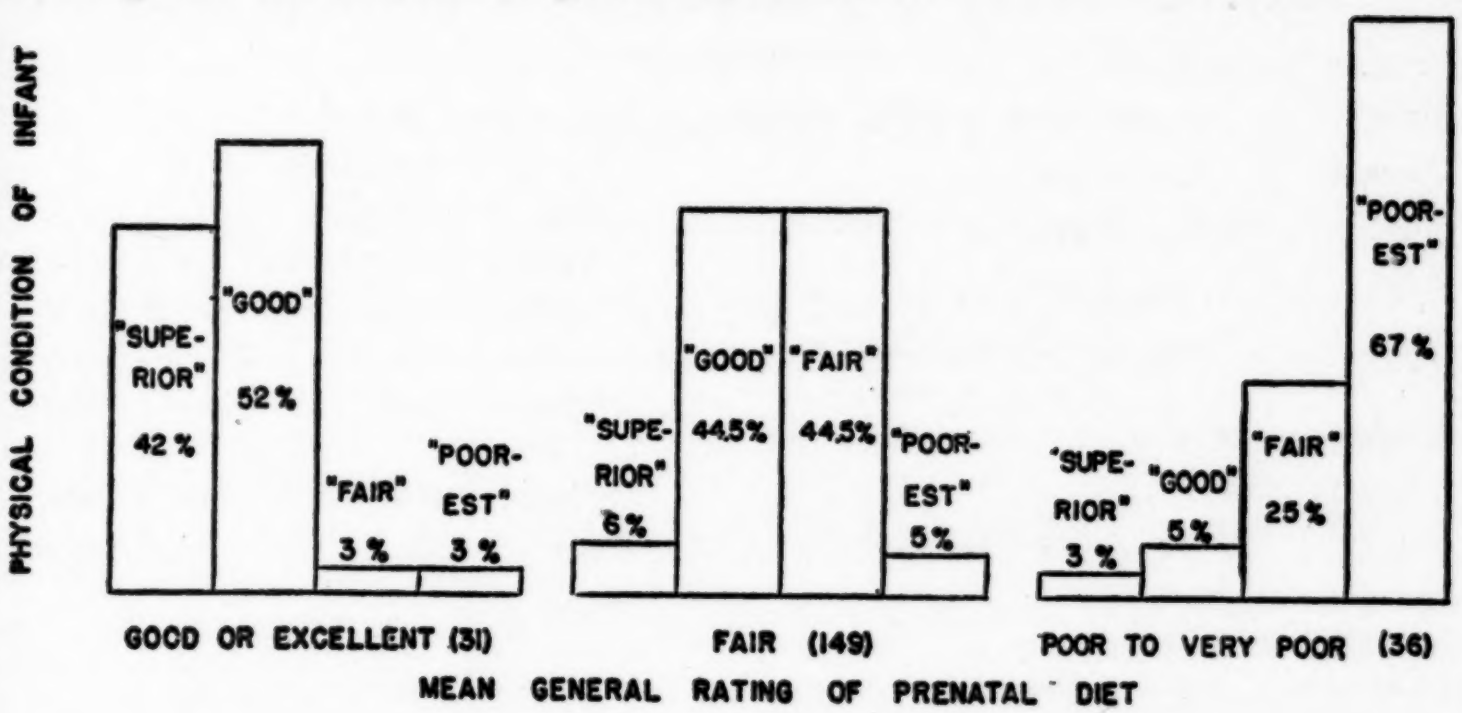
"excellent" or "good"; 17 per cent had "fair to good" diets; 29 per cent had "fair" diets; 23 per cent "fair to poor" diets; and 17 per cent had "poor to very poor" diets. This means that at least 40 per cent of these women were definitely malnourished during the period when the fetus undergoes very rapid growth and development, and that another 29 per cent had only mediocre diets for this period.

The infants were rated at birth and during the first two weeks of life on the basis of weight, length, general appearance and physical condition, health, progress and the like. The ratings of the infants ("superior," "good," "fair," "poorest") were then correlated with the ratings of the mothers' prenatal diets.



Relationship of prenatal nutrition to the physical condition of the infant at birth and within first 2 weeks of life. (Cases selected on the basis of mean rating assigned to mothers' diets during pregnancy, 216 cases).

From these studies the authors draw the following conclusions:

1. If the diet of the mother during pregnancy is poor to very poor, she will undoubtedly have an infant whose physical condition will be poor. In the 216 cases considered, all stillborn infants, all infants who died within a few days of birth except one, most infants who had marked congenital defects, all premature, and all functionally immature infants were born to mothers whose diets during pregnancy were very inadequate.
2. If the mother's diet during pregnancy is good or excellent, her infant will in all probability be in good or excellent physical condition. It may, however, happen rarely that a mother whose diet during pregnancy is good or excellent will give birth to an infant in poor physical condition (1 out of 216 cases in this study).

Dietary Recommendations:

The recent promulgation by the National Research Council of recommended dietary allowances during the latter half of pregnancy should provide a helpful guide in planning adequate diets.

Recommended Daily Allowances of Dietary Essentials for Women

	Calories	Protein, Gm.	Calcium, Gm.	Iron, Mg.
Woman, 56 Kg., nonpregnant	2,500	60	0.8	12
Pregnancy (latter half)	2,500	85	1.5	15

	Vitamins					
	A, I. U.	B_1, Mg.	C, Mg.	Riboflavin Mg.	Nicotinic Acid, Mg.	D, I. U.
Woman, 56 Kg., nonpregnant..	5,000	1.5	70	2.2	15	?
Pregnancy (latter half)	6,000	1.8	100	2.5	18	400-800

(Formulated by the Food and Nutrition Board of the National Research Council, 1941.)

If these dietary allowances are to be met the following foods in approximately the amounts specified must be provided daily (18):

Milk	— 40 ounces (2½ pints)	Yellow or green leafy vegetables (carrots, string beans, watercress)	— 1 serving
Cheese	— 1 ounce	Orange juice	— 3 ounces
Butter	— 2 ounces	or	
Egg	— 1 serving	Tomato juice	— 7 ounces
Meat	— 1 serving (liver once a week)	or	
Whole grain or enriched bread	— 4 slices	Grapefruit juice	— 4 ounces
Whole grain or restored cereal	— 1 serving	Other fruits	— 1 serving
Potato	— 1 serving	Vegetable such as cabbage or tomato	— 1 serving

Extra necessary calories may be provided by other foods according to individual needs and tastes. Vitamin D supplements providing at least 400–800 units daily, and preferably more, should also be included. At least one-half the protein intake should be derived from meat, eggs and dairy products such as milk, cheese and ice cream.

The combined results of prenatal diet studies both here and abroad have pointed out two important facts; (1) The quality of the diet during this physiologically important period markedly influences not only the course of pregnancy and the health of the mother, but the condition of the infant at birth and its health at least six months thereafter; (2) The diet of a majority of expectant mothers falls far short of meeting desirable nutrition goals during this critical period.

The findings reported emphasize the fact that an adequate diet in pregnancy is an important public health measure demanding more general professional and official recognition. There is a vital need of informing and aiding prospective mothers in obtaining the proper

diet during the prenatal period for successful childbearing. Education and the increasing policy of fortifying basic foods, such as flour, milk and cereals, represent a major step forward in this direction. Prenatal nutrition, now only in its beginnings as a specialized science, promises to develop into a significant public health problem with ramifications far beyond its present scope. The increased health and safety of mothers and the known benefits to the infant at birth and during the early months of life have already been indicated as the rewarding results of improved nutrition. The lifelong benefits to the child endowed with a superior nutritional background from prenatal days is but one example of what future studies may be expected to reveal.

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NEWS DIGEST

VITAMINS IN VARIETY MEATS—Analysis of beef liver and tongue, veal heart, Canadian bacon, bologna, frankfurters, other sausages, oxtail, lamb shank and other variety meats for thiamin, riboflavin and nicotinic acid reveals that they are a good source of these vitamins, containing about the same amounts as fresh muscle meats. Retention of these vitamins in some of the meats was studied during broiling, braising and boiling. Greater amounts of all the vitamins were retained after broiling than after braising. In the case of boiling, vitamin retention was dependent on the cooking time. In almost all instances more than 90 per cent of the nicotinic acid and riboflavin was recovered in the meat and drippings.—*J. Nutr. 28,* 35 (1944).

RIBOFLAVIN BIOSYNTHESIS—Recent studies on human subjects indicates that riboflavin, as well as thiamin, may be synthesized in significant amounts by bacterial action in the intestine. Twelve boys fed a special diet of purified vitamin-free foods plus supplements of pure vitamins subsisted for twelve weeks on a riboflavin intake restricted to 60—90 micrograms per day (as compared to a recommended daily allowance of from 1.8 to 3.0 milligrams for persons in this age group). Excellent health and weight maintenance were evidenced throughout. After a preliminary drop the urinary excretion of the vitamin tended to remain constant at a level almost twice that of the riboflavin intake. The fecal excretion remained constant at a level five to six times the intake, a phenomenon which is interpreted as evidence of synthesis of the vitamin by intestinal bacteria. Unlike the case with thiamin, intestinal synthesis of riboflavin does not appear to be affected by administration of certain sulfonamides. Whether biosynthesis of riboflavin would occur in the complete dietary absence of the vitamin remains to [illegible] investigated. The present experime[nt] does indicate, however, intestinal b[io]synthesis of riboflavin in man and po[ssi]bly therefore, the problem of reevaluati[on] the present accepted dietary requi[re]ment for this vitamin.—*J. Am. Me[d.] Assoc. 126,* 357 (1944).

SOY PROTEIN — One of the fi[rst] studies on digestibility and biologic[al] value of soybean protein in adult hu[man] subjects has recently been reporte[d]. It was found that average digestibiliti[es] in adults of the protein of cooked whol[e] soybeans, cooked soy flour and soymi[lk] are 90.5, 94.0 and 89.6 per cent, respe[c]tively. The biological value of soy pr[o]tein for maintenance in adults usi[ng] whole egg protein as a standard is 94 per cent for cooked whole soybean[s], 91.7 per cent for cooked soy flour an[d] 95.3 per cent for a commercial soymil[k]. —*J. Nutr. 28,* 209 (1944).

VITAMINS IN HAIR—A new meth[o]od whereby the vitamin content of hai[r] may be determined has been used t[o] obtain interesting data with respect t[o] the content of various B vitamins i[n] human hair and in the hair of experi[-] mental animals. Riboflavin, nicotini[c] acid, pantothenic acid and inositol o[c]cur in normal rat and human hair i[n] about the same ratio to each other a[s] they do in other tissues. Human hai[r] has a lower content of the vitamin[s] than rat hair. The vitamin content o[f] rat hair was found to be influenced b[y] diet. Limited studies of the relation o[f] baldness to the vitamin content of hu[-] man hair showed low inositol values i[n] certain instances. Further studies ar[e] necessary to establish the significanc[e] of these findings and the relation, i[f] any, of hair vitamin content to graynes[s] and baldness.—*J. Biol. Chem. 155,* 28[5] (1944).